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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,630	10/31/2003	Thomas C. Evans	NEB-211-US	3372
28986	7590	09/19/2006	EXAMINER	
HARRIET M. STRIMPEL; NEW ENGLAND BIOLABS, INC. 240 COUNTY ROAD IPSWICH, MA 01938-2723			PAGE, BRENT T	
		ART UNIT	PAPER NUMBER	
		1638		

DATE MAILED: 09/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)
	10/698,630	EVANS ET AL.
	Examiner Brent Page	Art Unit 1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 30 June 2006.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-43 is/are pending in the application.
- 4a) Of the above claim(s) 23,24,27-31,33-37 and 40-43 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-22,25,26,32,38 and 39 is/are rejected.
- 7) Claim(s) 15 and 16 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 29 March 2004 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>09/17/2004</u> .	6) <input checked="" type="checkbox"/> Other: <u>IDS 02/14/2005</u> .

DETAILED ACTION

Applicant's election of Group I in the reply filed on 06/30/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The withdrawal of claims 23-24, 27-31, 33-37 and 40-43 from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim is acknowledged. Election was made **without** traverse in the reply filed on 06/30/2006.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. There are three instances of embedded hyperlinks occurring in paragraphs 116, 167 and 169 of the specification. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claims 15 and 16 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. These claims fail to further limit the parent claim because

they refer to the limitation "the protein" that is not recited in the parent claim. In the interest of compact prosecution the claims have been treated on the merits. Such treatment does not relieve Applicant of the responsibility to respond to this objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-22, 25-26, 32 and 38-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn to a method for translocating an RNA into a chloroplast comprising contacting a chloroplast with an RNA comprising a first RNA sequence consisting of any chloroplast localization sequence, and a second RNA sequence characterized by its non-natural association with the first RNA sequence, and translocating the RNA into the chloroplast.

In contrast, the specification only provides guidance for very specific sequence embodiments of only Avocado Sunblotch Viroid sequence as a chloroplast localization sequence, specifically nucleotides 1-164 of SEQ ID NO: 3, nucleotides 84-247 of SEQ ID NO: 3, and SEQ ID NO: 3 with a deletion of nucleotides 83-165. The specification does not provide guidance for any other

embodiments of Avocado Sunblotch Viroid sequence as a chloroplast localization sequence, or guidance for any other chloroplast localization sequence from any other source as broadly claimed. The specification further only provides guidance for the transformation of plant cells with DNA constructs in relation to "contacting a chloroplast with RNA" and does not provide guidance for any other method of contacting the chloroplast with RNA. Similarly the specification only provides guidance for the translocation of RNA into a chloroplast by transformation of a DNA construct comprising specifically nucleotides 1-164 of SEQ ID NO: 3, nucleotides 84-247 of SEQ ID NO: 3, or SEQ ID NO: 3 with a deletion of nucleotides 83-165. The specification does not provide guidance for any other method steps or any other sequences that would successfully translocate RNA into the chloroplasts.

Organellar translocation of RNA is unpredictable, and the sequences responsible for translocation are not currently known in the art. In a review of mRNA localization in plants, Okita et al (2002 Current Opinion in Plant Biology 5: 553-559) state "The zip codes, which are usually located on the RNA's 3' untranslated region (UTR), may be sequence specific or structural, the latter complicating the identification of such signals by bioinformatics" (see page 553, second column end of second paragraph). Okita et al further address specifically, the targeting of mRNAs to organelles, specifically those of mitochondria and chloroplasts, and disclose that although RNAs are imported into the chloroplasts it is currently unclear whether the targeting is a result of specific sequence signals, localized protection of RNAs and/or the selective

degradation of RNAs that are localized in the cytoplasm (see page 555 first column, last paragraph for example).

In a review of protein targeting focusing on the importance of RNA localization, Crofts et al (2004 Plant Physiology 136: 3414-3419) state "To date, no general consensus sequences have been identified for RNA localization signals, and it is widely believed that the targeting process is likely to be more complex than first anticipated, with constant reorganization of the mRNA-protein complex en route to its final destination" (see page 3415 first column second half of third paragraph).

Given the state of the art, the disclosures by Okita et al and Crofts et al, and the lack of guidance as discussed above, it would be undue experimentation for one of skill in the art to isolate all RNA sequences that can act as chloroplast localization signals and evaluate such sequences for their ability to translocate the RNA to the chloroplasts as broadly claimed.

Claims 1-22, 25-26, 32 and 38-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a method for translocating an RNA into a chloroplast comprising contacting a chloroplast with an RNA comprising a first RNA sequence consisting of any chloroplast localization sequence, and a second

RNA sequence characterized by its non-natural association with the first RNA sequence, and translocating the RNA into the chloroplast.

In contrast, the specification only provides guidance for very specific sequence embodiments of only Avocado Sunblotch Viroid sequence as a chloroplast localization sequence, specifically nucleotides 1-164 of SEQ ID NO: 3, nucleotides 84-247 of SEQ ID NO: 3, and SEQ ID NO: 3 with a deletion of nucleotides 83-165. The specification does not provide guidance for any other embodiments of Avocado Sunblotch Viroid sequence as a chloroplast localization sequence, or guidance for any other chloroplast localization sequence from any other source as broadly claimed.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id. Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." Id.

Finally, the court held:

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Id.*

See also MPEP section 2163, page 174 of chapter 2100 of the August 2005 version, column 1, bottom paragraph, where it is taught that

[T]he claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

See also *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at 1021, (Fed. Cir. 1991) where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

Given the claim breadth and lack of guidance as discussed above, the specification fails to provide an adequate written description of the genus of sequences as broadly claimed. Given the lack of written description of the claimed genus of sequences, any method of using them, such as transforming plant cells and plants therewith, and the resultant products including the claimed transformed plant cells and plants containing the genus of sequences, would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicant to have been in possession of the claimed invention at the time of filing. See the Written Description Requirement guidelines published in Federal Register/ Vol. 66, No. 4/ Friday January 5, 2001/ Notices: pp. 1099-1111.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-14, 17-19, 20-21, 25-26, and 38-39 are rejected under 35 U.S.C. 102(e) as being anticipated by Waterhouse et al (US Patent 6423885 filed 08/13/1999).

The claims are broadly drawn to a method for translocating an RNA into a chloroplast comprising contacting a chloroplast with an RNA comprising a first RNA sequence consisting of any chloroplast localization sequence (CLS) wherein the CLS shares substantial homology with a viroid or at least part of a viroid, and a second RNA sequence characterized by its non-natural association

with the first RNA sequence, wherein the second RNA sequence encodes a whole or "a part" of a target protein, wherein the second RNA sequence is less than 10 kb and wherein the RNA is a product of transcription of DNA and translocating the RNA into the chloroplast. The claims are further drawn to a virus containing an RNA or DNA encoding an RNA sequence which is substantially homologous to a segment of an avocado sunblotch viroid and a plasmid containing a DNA encoding an RNA sequence which is substantially homologous to a segment of an avocado sunblotch viroid.

Waterhouse et al teach a method in which a tobacco plant is transformed with viral vector comprising an avocado sunblotch viroid, a second RNA sequence that is a targeting sequence that inherently encodes at least "part of" a target protein wherein the "part" is interpreted as little as a single amino acid and wherein it is inherent that the two RNA sequences have untranslated RNA located between them as the second RNA sequence does not contain a start codon, wherein the second RNA sequence is less than 10 Kb. The viral vector comprises the DNA sequence of the above described sequence that is transcribed in the nucleus of the cell. It is an inherent property of transforming the above with a viral vector that some of the DNA transformed will be present in the cytoplasm of the transformed plant cell. The translocation of the RNA transcribed to the chloroplast would be an inherent property of the transcribed RNA given the localization of avocado sunblotch viroid to the chloroplasts (see claims 1, 4, 11-13, and Column 3 in its entirety, as well as column 18 lines 54-67 and column 19 lines 1-5 for example).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-19, 20-22, 25-26, and 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waterhouse et al (US Patent 6423885 filed 08/13/1999) in view of Sanford et al (US Patent 5036006).

In addition to the claim interpretation in the above 102 rejection, the claims are also drawn to the same wherein the DNA is introduced into the plant cell by a physical or chemical means.

Waterhouse et al teach a method in which a tobacco plant is transformed with viral vector comprising an avocado sunblotch viroid, a second RNA sequence that is a targeting sequence that inherently encodes at least “part of” a target protein wherein the “part” is interpreted as little as a single amino acid and wherein it is inherent that the two RNA sequences have untranslated RNA located between them as the second RNA sequence does not contain a start codon, wherein the second RNA sequence is less than 10 Kb. The viral vector comprises the DNA sequence of the above described sequence that is transcribed in the nucleus of the cell. The translocation of the RNA transcribed to the chloroplast would be an inherent property of the transcribed RNA given the localization of avocado sunblotch viroid to the chloroplasts. Waterhouse et al

also mention that alternative transformation methods such as particle bombardment may be used instead of the viral vector method (see claims 1, 4, 11-13, and Column 3 in its entirety, as well as column 18 lines 54-67 and column 19 lines 1-5 for example).

Waterhouse et al do not teach the transformation of tobacco plants with the particle bombardment method.

Sanford et al teach the particle bombardment method of transforming tobacco plant cells (see 1-13 for example).

Given the state of the art and the disclosures by Waterhouse et al and Sanford et al, it would have been obvious to one of ordinary skill in the art to modify the method taught by Waterhouse et al by using particle bombardment for transformation taught by Sanford et al, as suggested by Waterhouse et al.

Claim 32 is free of the prior art given the failure of the prior art to teach or reasonably suggest the above method wherein the second RNA sequence is expressed as protein in the chloroplast.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brent Page whose telephone number is (514)-272-5914. The examiner can normally be reached on Monday-Friday 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571)-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brent T Page

DAVID T. FOX
PRIMARY EXAMINER
GROUP 180-1638

